

**Amendment and Response**

Applicant: Winthrop D. Childers et al.

Serial No.: 10/808,945

Filed: March 25, 2004

Docket No.: 200314152-1

Title: METHOD OF SORTING CELLS ON A BIODEVICE

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**IN THE CLAIMS**

Please cancel claims 2-3, 21, and 29.

Please amend claims 1, 4-8, 13-16, 18-20, 22-23, and 25-28 as follows:

1. (Currently Amended) A micro-filtration device for sorting cells comprising:  
an apparatus including a barrier structure defining an array of openings arranged within a fluid flow path, the openings having at least one of a size and a shape configured to direct only a portion of the cells through the openings based on at least one of a size and a shape of each cell; and  
an electrode arrangement disposed about the array of openings and configured to apply an non-uniform electric field to enhance passagedirection of the portion of the cells through the openings, wherein the electrode arrangement is separate from, and independent of, the barrier structure.

2-3. (Canceled)

4. (Currently Amended) The device of claim 31, wherein the fluid flow path is configured to conduct cells in a first direction to move the cells through the apparatus, and wherein the electrode arrangement is arranged to generate the non-uniform electric field as a temporally varying non-uniform electric field to move the portion of the cells, after passage through the barrier structure, in a second direction generally transversedifferent from to the first direction.

5. (Currently Amended) A micro-filtration device for sorting cells comprising:  
an apparatus including a barrier structure defining an array of openings arranged within a fluid flow path, the openings having at least one of a size and a shape configured to direct only a portion of the cells through the openings based on at least one of a size and a shape of each cell, wherein the fluid flow path is configured to conduct cells in a first direction to move the cells through the apparatus; and

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an electrode arrangement disposed about the array of openings and configured to apply a non-uniform electric field to enhance direction of the portion of the cells through the openings, wherein the electrode arrangement is arranged to generate the non-uniform electric field as a temporally varying non-uniform electric field in a second direction different from the first direction;

~~The device of claim 4, wherein the openings comprise~~include:

a first set of openings permitting passage of cells of a first size in the first direction;

a second set of openings permitting passage of cells of a second size, smaller than the first size, in the first direction; and

a third opening extending transversely between the first and second set of openings, and permitting movement of cells of the first size in the second direction; and

wherein the electrode arrangement comprisesincludes a first electrode array extending within the third opening and configured to apply the temporally varying non-uniform electric field to move cells of the first size in the second direction, which is transverse to the first direction of the fluid flow path, away from the first and second set of openings.

6. (Currently Amended) A micro-filtration device for sorting cells comprising:  
an apparatus including a barrier structure defining an array of openings arranged within a fluid flow path, the openings having at least one of a size and a shape configured to direct only a portion of the cells through the openings based on at least one of a size and a shape of each cell, wherein the fluid flow path is configured to conduct cells in a first direction to move the cells through the apparatus; and

an electrode arrangement disposed about the array of openings and configured to apply a non-uniform electric field to enhance direction of the portion of the cells through the openings, wherein the electrode arrangement is arranged to generate the non-uniform electric field as a temporally varying non-uniform electric field in a second direction different from the first direction;

~~The device of claim 4, wherein the barrier structure comprises:~~

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a plurality of barrier arrays aligned generally parallel to each other to define a succession of barrier arrays, each successive barrier array defining a smaller set of passages to progressively sort cells in decreasing size into different respective portions as the cells move in the fluid flow path in the first direction; and

a plurality of transport paths disposed between and extending transversely to the successive barrier arrays with each transport path including one of a plurality of [[an]] electrode arrays of the electrode arrangement, ~~the~~each respective electrode array configured to apply the temporally varying non-uniform electric field to move the respective portion of the cells through each respective transport path in the second direction.

7. (Currently Amended) The device of claim 31, wherein the openings have an elongate shape and the electrode arrangement is arranged to ~~form~~apply the non-uniform electric field in substantially alignment with the elongate shape of the openings.

8. (Currently Amended) A micro-filtration device for sorting cells comprising:  
an apparatus including a barrier structure defining an array of openings arranged  
within a fluid flow path, the openings having at least one of a size and a shape configured to  
direct only a portion of the cells through the openings based on at least one of a size and a  
shape of each cell, wherein the openings have an elongate shape; and  
an electrode arrangement disposed about the array of openings and configured to  
apply a non-uniform electric field to enhance direction of the portion of the cells through the  
openings, wherein the electrode arrangement is arranged to apply the non-uniform electric  
field in substantial alignment with the elongate shape of the openings;

~~The device of claim 7, and~~ wherein the array of openings comprises:

a first set of openings wherein the electrode arrangement straddles the first set of openings to apply the non-uniform electric field to substantially align a long axis of the cells with a long axis of the openings of the first set of openings.

9. (Original) The device of claim 8, wherein the electrode arrangement comprises:

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a first pair of electrodes including a first electrode and a second electrode, the first electrode and the second electrode disposed on opposite sides of the first set of openings and configured to apply the non-uniform electric field.

10. (Currently Amended) The device of claim 9, wherein the first electrode is disposed above the first set of openings and the second electrode is disposed below the first set of openings to apply the non-uniform electric field as a first non-uniform electric field.

11. (Original) The device of claim 9, wherein the first electrode is disposed at an entrance of the first set of openings and the second electrode is disposed at an exit of the first set of openings to apply the non-uniform electric field as a second non-uniform electric field.

12. (Currently Amended) The device of claim 9, wherein the first electrode is disposed above the first set of openings and the second electrode is disposed below the first set of openings to apply the non-uniform electric field as a first non-uniform electric field; and wherein the electrode arrangement further comprises:

a second pair of electrodes with a first electrode and a second electrode, wherein the first electrode of the second pair of electrodes is disposed adjacent an entrance of the first set of openings and the second electrode of the second pair of electrodes is disposed adjacent an exit of the first set of openings to apply the non-uniform electric field as a second non-uniform electric field.

13. (Currently Amended) A micro-filtration device for sorting cells ~~The device of claim 1, further comprising:~~

an apparatus including a barrier structure defining an array of openings arranged within a fluid flow path, the openings having at least one of a size and a shape configured to direct only a portion of the cells through the openings based on at least one of a size and a shape of each cell;

an electrode arrangement disposed about the array of openings and configured to apply an electric field to enhance direction of the portion of the cells through the openings; and

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at least one of an acoustic device and an electric device with each respective device configured to apply a force to the cells traveling along the fluid flow path to prevent aggregation of the cells within the apparatus.

14. (Currently Amended) A cell sorter chip comprising:  
means for sorting cells based on a plurality of dimensions of the cells; and  
means for electrically enhancing the sorting of cells,  
wherein the means for sorting and the means for electrically enhancing the sorting together comprise at least one of:

a first filtration device that sorts cells according to their sizes, wherein the first filtration device is succeeded within a fluid flow path by a second filtration device that sorts cells according to their dimensional orientation; or

a third filtration device that sorts cells according to their dimensional orientation, wherein the third filtration device is succeeded within the fluid flow path by a fourth filtration device that sorts cells according to their sizes.

15. (Currently Amended) The chip of claim 14, wherein the means for sorting cells each of the respective first, second, third and fourth filtration devices comprises:  
a substrate having a barrier structure defining openings.

16. (Currently Amended) A cell sorter chip The chip of claim 15, comprising:  
means for sorting cells based on a plurality of dimensions of the cells, the means for sorting including a substrate having a barrier structure defining openings, wherein the openings each have a long axis; and  
means for electrically enhancing the sorting of cells, including the means for electrically enhancing the sorting comprises an electrode array disposed and arranged to generate an electric field to align a long axis of the cells with the long axis of the openings.

17. (Original) The chip of claim 16 wherein the electric field is a non-uniform electric field.

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18. (Currently Amended) The chip of claim 15, ~~wherein the barrier structure defines an area of filtration on the substrate,~~ wherein the means for electrically enhancing the sorting comprises an electrode array disposed and arranged to convey the cells away from the respective first, second, third, and fourth filtration devices ~~area of filtration~~.

19. (Currently Amended) A cell sorter chip ~~The chip of claim 15, further comprising:~~ means for sorting cells based on a plurality of dimensions of the cells, including a substrate having a barrier structure defining openings;

means for inducing a fluid flow on the substrate in a first direction along a path of the fluid flow ~~and through the openings;~~ and

~~wherein the~~ means for electrically enhancing the sorting of cells ~~is disposed for via~~ transporting the cells in a second direction to a location out of the fluid flow.

20. (Currently Amended) The chip of claim 19, wherein the means for electrically enhancing the sorting comprises an electrode array disposed and arranged to apply a temporally varying non-uniform electric field to transport a certain size range of cells out of ~~from the fluid flow path.~~

21. (Canceled)

22. (Currently Amended) The chip of claim 214, wherein the means for electrically enhancing the sorting comprises:

a first electrode arrangement configured to apply a temporally varying non-uniform electric field in at least one of the first filtration device or the fourth filtration device to move groups of cells, sorted according to their respective sizes, out of the at least one of the first filtration device or the fourth filtration device, respectively; and

a second electrode arrangement configured to apply an electric field in at least one of the second filtration device or the third filtration device to permit cell passage within the at least one of the second filtration device or the third filtration device, respectively, by causing at least one dimension of the cells to become aligned with a gap that has a shape and a size substantially matching the at least one dimension of the cells.

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23. (Currently Amended) A method of sorting cells on a biodevice comprising:  
directing a flow of cells within a fluid into a filtration structure defining an array of fluid openings; and  
encouraging cell passage of each cell of a portion of the cells through the fluid openings based on at least one dimension of each cell via application of ~~an~~ non-uniform electric field within the fluid openings.
24. (Original) The method of claim 23, wherein encouraging cell passage comprises:  
aligning each cell in the portion of the cells relative to the fluid openings.
25. (Currently Amended) ~~The method of claim 24~~ A method of sorting cells on a biodevice comprising:  
directing a flow of cells within a fluid into a filtration structure defining an array of fluid openings, wherein the fluid openings include an elongate shape, each fluid opening has a major axis substantially perpendicular to a direction of fluid flow through the fluid openings, and each cell has at least one major axis; and ~~wherein aligning each cell comprises:~~  
~~encouraging cell passage of each cell of a portion of the cells through the fluid openings based on at least one dimension of each cell via application of an electric field within the fluid openings applying the electric field to align the at least one major axis of each cell with the major axis of one of the fluid openings.~~
26. (Currently Amended) The method of claim 25, wherein the at least one major axis includes two major axes and each cell has the two major axes and a minor axis.
27. (Currently Amended) The method of claim ~~[[24]]~~25, wherein the at least one major axis of each cell defines~~has~~ one major axis and ~~a direction of passage through the fluid openings~~, wherein encouraging cell passage comprises: aligning the one major axis of each cell with ~~[[the]]~~a direction of passage through the fluid openings.

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28. (Currently Amended) A method of sorting cells on a biodevice comprising:

~~The method of claim 23, wherein directing the flow of cells comprises:~~

directing a flow of cells within a fluid into a filtration structure defining successive arrays of fluid openings;

separating the cells as the cells flow through the successive arrays of fluid openings with each successive array of fluid openings having decreasing dimensions to sort the cells into different groups based on their size; and wherein encouraging cell passage comprises:

encouraging cell passage of each cell of a portion of the cells through the respective fluid openings based on at least one dimension of each cell via application of a first non-uniform electric field within the fluid openings; and

moving the different groups of cells in independent, generally parallel pathways in a direction generally transverse to the flow of cells through the array of fluid openings by application of the electric field as a temporally varying second non-uniform electric field along each respective pathway.

29. (Canceled)